ABSTRACT

New tools for determining the role the α_{1B} adrenergic receptor plays in the physiology and pathology of the brain and the cardiovascular system are provided. The tools are transgenic non-human mammalian animals, particularly transgenic mice, that have integrated into the genomes of their somatic cells a transgene encoding an exogenous, wild-type α1B adrenergic receptor or a variant thereof. The transgenic animals of the present invention exhibit phenotypical symptoms similar to those exhibited by individuals with neurodegenerative diseases, particularly Parkinson's disease or epilepsy. Such mammals also exhibit phenotypical symptoms similar to individuals with cardiovascular diseases such as hypertrophy of the heart and hypotension. Accordingly, these transgenic mammals are also useful for screening for drugs that ameliorate these cardiovascular conditions. Also provided is a method of determining the ability of a test agent or compound to modulate or block function of the α_{1B} adrenergic receptor. The method comprises administering the test agent to a transgenic non-human animal which is expressing a constitutively active form of the α_{1B} receptor, or elevated levels of the wild-type α_{1B} receptor on the cell surface of various organs, and then assaying for changes in α_{1B} receptor function. The present invention also relates to methods for treating neurodegenerative disorders in a subject, particularly neurodegenerative disorders evidenced by abnormal locomoter activity or seizures. In one embodiment, the method comprises administering a pharmaceutical composition comprising a biologically effective amount of an α_1 adrenergic receptor antagonist to the subject.